

## Quantitative Analysis of Polyethylene Glycols by Gas Chromatography after Silylation

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Quantitative analysis of polyethylene glycols by temperature-programmed gas chromatography after silylation has shown that the molecular weight distribution closely follows a Poisson distribution function only for polyethylene glycols with a very low degree of polymerisation. Polyethylene glycols with an average molecular weight in the range of 200–400 show a narrower distribution.

Flory assumed that all steps in the reaction between ethylene glycol and ethylene oxide proceed with equal rate, and showed that the molecular weight distribution of the resultant polyethylene glycol mixture could be described by a Poisson function.<sup>1</sup> Weibull and Nycander found this to be true for the oxyethylation of ethylene glycol and its monoethyl ether with one mole of ethylene oxide.<sup>2</sup> The distribution of higher polyethylene glycols has not been studied by direct quantitative analysis of all components in the reaction mixture. A semi-quantitative evaluation has indeed been carried out after conversion of polyethylene glycol into the corresponding methyl ethers.<sup>3</sup> However, this technique has not revealed quantitative information regarding the higher members of the series.

Recently, we have found that the molecular weight range available for analysis could be greatly extended by silylation of oxyethylation mixtures\* before separation by gas chromatography.<sup>4</sup> Results obtained by the application of this technique on the quantitative analysis of polyethylene glycols in the average molecular weight range of 100–400 are now presented.

### EXPERIMENTAL

*Materials.* Reference substances and internal standards were purified by vacuum distillation to a purity of better than 99.5 % (found by gas chromatography). Trimethylchlorosilane and hexamethyldisilazane were obtained from Dow Corning Corp. and distilled before use.

\* Some examples of the application on various ethylene oxide adducts were presented by the author at the Third Scandinavian Symposium on Surface Chemistry, Fredensborg, Denmark, January 12–13th 1967.

*Silylation technique.* Model experiments with di- and tetraethylene glycol showed that a slight degradation of the polyether chain might occur under the conditions used before.<sup>4</sup> The following procedure was found to be suitable. To a 200 mg sample in a dry test tube 1.0 ml each of hexamethyldisilazane and trimethylchlorosilane was added. The tube was sealed with Teflon tape, shaken vigorously for 15 sec and allowed to stand at room temperature for 5 min. Dry benzene (1 ml) was added and the mixture shaken again. The tube was centrifuged, and a sample of the solution was taken, (using a syringe through the Teflon tape) and analysed by gas chromatography.

*Gas chromatography.* A Perkin-Elmer 800 Gas Chromatograph, (equipped with a dual column system and differential flame ionization detector) was used with short columns (1/4 inch  $\times$  2 feet) made from stainless steel. The columns contained 2 % preheated Dow Corning High Vacuum Grease on Chromosorb G (45 – 60 mesh). In order to avoid local overheating of the stationary phase, the columns were packed so that 5 cm of the column end connected to the injection block was free of stationary phase, thus containing solid support only. The stationary phase material was preheated at 350°C and 2 mm Hg for 4 h. (This treatment positively affected the base line stability and the material's length of life). The injection block temperature was kept at 430°C during the separations. Column temperature was programmed with a gradient of 10.4°C/min from the starting temperature, 60°C. The carrier gas flow was 70 ml N<sub>2</sub>/min through both columns, measured at room temperature. Using the instrument regulators the gas flow was adjusted at the highest column temperature so that a stable base line was obtained over the entire temperature range. The split ratio was 1:4 and the sample amount 2  $\mu$ l. Detector sensitivity  $2 \times 10^2$  to  $10^3$ . Relative retention data are found in Table 1.

Table 1. Response factors and relative retention.

Glycol <sup>a</sup> <i>n</i>	Response factor $C_F$		Relative retention <sup>b</sup>
	dodecanol	hexadecane	
1	0.62 $\pm$ 0.02	0.54	0.11
2	0.94 $\pm$ 0.02	0.82	0.41
3	1.16 $\pm$ 0.03	1.04	0.83
4	1.32 $\pm$ 0.03	1.18	1.21
5	1.41	1.28	1.53
6	1.49		1.82
7	1.53		2.09
8	1.53		2.33
9	1.62		2.57
10			2.76
11			2.95
12			3.12
13			3.28

<sup>a</sup> HO(CH<sub>2</sub>CH<sub>2</sub>O)<sub>*n*</sub>H.

<sup>b</sup> Hexadecane (6.5 min) = 1.00.

*Quantitative analysis.* Peak areas were calculated by the height  $\times$  width at half height method. In order to obtain chromatograms with suitable peak widths, the recorder (Hitachi-Perkin Elmer 159) was operated at the maximum speed (40 mm/min). The measurements were facilitated by the use of a small stand magnifier (11.5 dioptré units). Peak areas were multiplied with a specific response factor  $C_F$  defined as  $C_F = (W/A) \times (A_S/W_S)$  where  $A$  and  $A_S$  represent the peak area of the substance to be analysed and the internal standard, respectively.  $W$  and  $W_S$  represent the corresponding weight ratios. The internal standard, (10–15 % dodecanol-1 or hexadecane) was added to the

sample before the silylation. The response factors for the individual glycols were obtained by analysis of mixtures with known composition. The factors for pentaethylene glycol to nonaethylene glycol were determined by using the corresponding bis-trimethylsilyl ethers, isolated by preparative gas chromatography. The response factors for pentaethylene glycol and hexaethylene glycol were determined both with the individual glycols\* and the corresponding silyl ethers, which gave the same values. Response factors are given in Table 1. The standard deviation values shown in the table have been obtained by analysis on different occasions. They are based on 8–10 determinations for each glycol. The response factors do not change with the concentration in the range 5–80%, and the relative response values of the different glycols are independent of the kind of internal standard used. A plot of the response factors against the number of ethylenoxy groups shows that the response factor reaches a constant value at about 10 ethylenoxy units. Such calibration curves were used in the analysis of polyethylene glycols in which higher members than nonaethylene glycol were present.

*Preparative gas chromatography.* In order to obtain the response factors for some higher glycols than hexaethylene glycol, a preparative separation was carried out with Aerograph Autoprep A-700 (equipped with a hot-wire detector), using a 1/4" × 2 m aluminium column with 20% Dow Corning High Vacuum Grease on Chromosorb G. The gas flow was 90 ml He/min, and the temperature was programmed between 100 and 300°C with the instrument setting 70. The amount injected was 400 μl per pass and the detector sensitivity 64. Polyethylene glycol with an average molecular weight of 300 (Mo och Domsjö Aktiebolag) was silylated as described above (increasing the scale 25 times). The fractions up to tetraethylene glycol were rejected and the silyl ethers of penta- to undecaethylene glycols were collected. Their purity was checked by elemental analysis and analytical gas chromatography. 20–150 mg of the silyl ethers of penta- to nonaethylene glycol were isolated in sufficient purity (Table 2). In determining the

Table 2. Isolated glycol silyl ethers.

$n^a$	Formula	Found		Calculated		Purity <sup>b</sup> %
		% C	% H	% C	% H	
5	C <sub>16</sub> H <sub>38</sub> O <sub>6</sub> Si <sub>2</sub>	49.6	9.2	50.2	10.0	99.0
6	C <sub>18</sub> H <sub>42</sub> O <sub>7</sub> Si <sub>2</sub>	50.0	9.5	50.7	9.9	98.7
7	C <sub>20</sub> H <sub>46</sub> O <sub>8</sub> Si <sub>2</sub>	51.1	9.6	51.0	9.9	97.4
8	C <sub>22</sub> H <sub>50</sub> O <sub>9</sub> Si <sub>2</sub>	52.6	9.5	51.3	9.8	95.6
9	C <sub>24</sub> H <sub>54</sub> O <sub>10</sub> Si <sub>2</sub>	52.4	9.4	51.6	9.7	94.8
10	C <sub>26</sub> H <sub>58</sub> O <sub>11</sub> Si <sub>2</sub>	44.3	8.5	51.8	9.7	—

<sup>a</sup> (CH<sub>3</sub>)<sub>3</sub>SiO(CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub>Si(CH<sub>3</sub>)<sub>3</sub>.

<sup>b</sup> Gas chromatography.

purity, the response factors found above for mono- to hexaethylene glycol were used. The purity decreases with increasing molecular weight. The decaethylene glycol silyl ether derivative was contaminated, probably by stationary phase "bleeding out" of the column.

*Preparation of polyethylene glycols.* A 2 l stainless steel autoclave, equipped with a high-speed conic stirrer was used in the preparation of polyethylene glycols from lower ethylene glycols and ethylene oxide. The oxyethylations were carried out at 170–180°C and 5 atm with a technique similar to the one described by Stockburger and Brandner.<sup>5</sup> Sodium hydroxide was used as a catalyst, which was neutralised with acetic acid after the reaction. For comparison, some oxyethylations were carried out without any catalyst

\* A gift of high-purity pentaethylene glycol and hexaethylene glycol from Dr. W. T. Weller, Unilever Research Laboratory, Port Sunlight, England, is gratefully acknowledged.

added. The average molecular weight of the adducts was calculated from hydroxyl group determinations with acetic anhydride.<sup>6</sup> Experimental details from the oxyethylations are shown in Table 3.

Table 3. Preparation of polyethylene glycols.

Expt. No.	Starting glycol		Ethylene oxide g	Catalyst concentration <sup>a</sup> %	Molecular weight <sup>b</sup>
	nature	g			
1	mono-	124	93.1	0.2	109
2	di-	212	85.8	0.2	151
3	tri-	70	23.7	0.2	198
4	mono-	124	89.3	0	109
5	mono-	100	225.4	0.02	205
6	mono-	100	391.8	0.02	297
7	mono-	100	380.0	0.2	288
8	mono-	100	228.3	0	201
9	di-	108	90.7	0.2	197
10 <sup>c</sup>	di-	318	586	0.2	304
11 <sup>c</sup>	di-	318	884	0.02	407

<sup>a</sup> Initial concentration in weight percent of glycol charged.

<sup>b</sup> As found by hydroxyl group determinations.

<sup>c</sup> Carried out at Research Laboratory, Mo och Domsjö Aktiebolag, Örnsköldsvik, Sweden.

*Calculation of theoretical molecular weight distribution.* The Poisson function is written  $n_i/n_{00} = e^{-v} \times (v^i/i!)$  with the same notations as were used by Weibull and Nycander.<sup>2</sup> Thus,  $n_{00}$  represents moles of starting material,  $n_i$  is the number of moles in the reaction

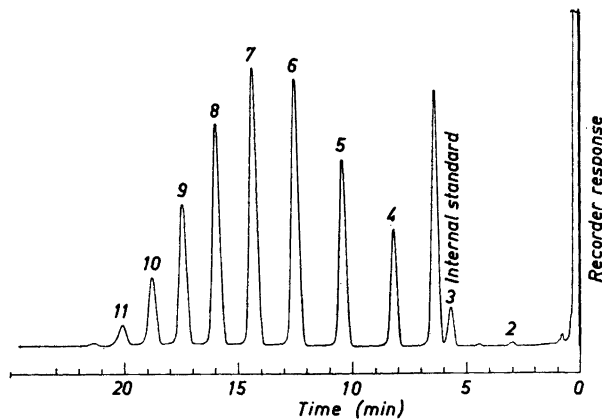


Fig. 1. Gas chromatogram of silylated polyethylene glycol with an average molecular weight of 300 (Expt. No. 6). The figures represent the number of ethylenoxy units in the glycols. Starting temperature: 70°C. Temperature programming: 10.4°C/min. Recorder speed: 10 mm/min. Sample volume: 3.0  $\mu$ l. Detector sensitivity:  $10^8$ . Internal standard: 12.7% dodecanol-1.

mixture of a component with  $i$  added ethylenoxy units, and  $v$  is the average molar ratio of ethylene oxide to starting material. The value  $v$  was calculated from the average molecular weight found by the hydroxyl group determination.

### RESULTS

The chromatogram in Fig. 1 shows the excellent separation obtained between the individual glycols present in polyethylene glycol with an average molecular weight of 300. Already the general appearance of this chromatogram seems to indicate that the components are distributed according to a Poisson-type distribution. However, a correct quantitative analysis requires calibration of the detector signal for all compounds in the mixture. By applying preparative gas chromatography on polyethylene glycol after silylation, it was possible to obtain the compounds necessary for this calibration. The calibration factors thus obtained are shown in Table 1.

The result of a quantitative analysis of a mixture of the four lowest members in the polyethylene glycol series is shown in Table 4. Maximum relative

Table 4. Quantitative analysis of ethylene glycols.

Glycol	Calculated (%)	Found by analysis <sup>a</sup> (%)	
		Mean value	Abs. standard deviation
Ethylene glycol	18.7	19.3	0.4
Diethylene glycol	28.8	28.9	0.2
Triethylene glycol	24.0	22.9	0.2
Tetraethylene glycol	28.5	27.2	0.4

<sup>a</sup> Internal standard: 18.3 % dodecanol-1. Five replicate analyses.

standard deviation from the mean value was found to be 2 % (for ethylene glycol). The net accuracy of the method is influenced by errors in the determination of the response factors as well as errors in the quantitative evaluation of the chromatograms. From the values given for these errors, the effective residual standard deviation<sup>7</sup> can be estimated to 1–3 % in duplicate analyses.

Polyethylene glycols with different average molecular weight were prepared from ethylene oxide and various lower glycols (Table 3). The composition of these were determined by duplicate analyses, and the results compared with the theoretical Poisson distribution. Table 5 shows that the oxyethylation of ethylene glycol and diethylene glycol with only one mole of ethylene oxide gives a mixture with the components distributed approximately according to a Poisson function, in accordance with earlier results.<sup>2</sup> (Expt. Nos. 1, 2,

Table 5. Comparison of the observed molecular weight distribution ( $n_i/n_{00}$ ) of polyethylene glycols with Poisson distribution.

Expt. No.	1 $v = 1.065$		2 $v = 1.02$		3 $v = 1.08$		4 $v = 1.065$		5 $v = 3.24$		6 $v = 5.33$		9 $v = 2.08$		10 $v = 4.49$		11 $v = 6.83$	
	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
0	0.345	0.375	0.361	0.357	0.340	0.376	0.345	0.351	0.039	0.017	0.005	0.005	0.125	0.079	0.011	0.003	0.001	0.002
1	0.367	0.363	0.368	0.393	0.367	0.422	0.367	0.370	0.127	0.073	0.026	0.006	0.260	0.252	0.050	0.039	0.007	0.004
2	0.195	0.215	0.188	0.196	0.197	0.222	0.195	0.218	0.205	0.221	0.069	0.045	0.270	0.282	0.113	0.115	0.025	0.018
3	0.069	0.067	0.065	0.060	0.071	0.047	0.069	0.070	0.222	0.273	0.122	0.118	0.187	0.194	0.169	0.174	0.059	0.037
4	0.019	0.008	0.018		0.020		0.019	0.007	0.180	0.215	0.163	0.175	0.097	0.108	0.190	0.231	0.098	0.099
5	0.004		0.003		0.007		0.004		0.117	0.131	0.174	0.225	0.041	0.038	0.171	0.208	0.134	0.172
6	0.001				0.001		0.001		0.063	0.056	0.154	0.194	0.014	0.006	0.128	0.143	0.153	0.206
7									0.029	0.014	0.118	0.152	0.004		0.082	0.076	0.149	0.191
8									0.012	0.002	0.078	0.079	0.001		0.046	0.028	0.127	0.143
9									0.004		0.047	0.021	0.001		0.023	0.004	0.096	0.092
10									0.001		0.025		0.001		0.010		0.066	0.044
11											0.012		0.004		0.004		0.041	0.014
12											0.005		0.002		0.002		0.023	0.003
13											0.002		0.001		0.001		0.012	
14											0.001						0.006	
15																	0.002	
16																	0.001	
$\sum_{i=0}^{16} n_i$	1.000	1.027	1.003	1.006	1.003	1.065	1.000	1.016	0.999	1.002	1.001	1.020	0.999	0.959	1.000	1.021	1.000	1.024
$\sum_{i=0}^{16} n_{00}$																		
M.W.		106		150		191		107		204		289		205		298		398

and 4). On the other hand, the oxyethylation of triethylene glycol under similar conditions resulted in a mixture with a narrower distribution (Expt. No. 3). The deviation from the theoretical values is much greater than the method's errors.

During an oxyethylation,<sup>5</sup> the catalyst concentration gradually decreases from its initial level. The influence of the catalyst concentration upon the composition of the reaction mixture is given in Table 6. No significant differ-

Table 6. The composition of polyethylene glycols prepared with different catalyst concentrations.

Glycol <sup>a</sup> <i>n</i>	Composition, % by weight					
	Expt. 5	No. 8	Theory <sup>b</sup> <i>v</i> = 3.20	Expt. 6	No. 7	Theory <sup>b</sup> <i>v</i> = 5.13
1	0.5	0.6	1.2	0.1	0.3	0.2
2	3.8	3.4	6.8	0.2	0.3	1.1
3	16.2	15.9	15.4	2.3	2.8	4.1
4	25.9	25.9	21.3	7.7	8.4	9.0
5	25.0	25.2	20.9	14.0	14.1	14.1
6	18.1	18.6	15.9	21.4	21.8	17.2
7	8.9	10.2	9.8	21.3	22.7	17.0
8	2.5	3.7	5.1	19.0	17.7	14.1
9	0.4	0.5	2.2	11.0	10.8	10.1
10	—	—	0.9	3.2	4.3	6.4
11			0.3	0.2	0.4	3.6
12			0.1			1.8
13						0.8
14						0.4
15						0.1

<sup>a</sup> HO(CH<sub>2</sub>CH<sub>2</sub>O)<sub>*n*</sub>H.

<sup>b</sup> Poisson.

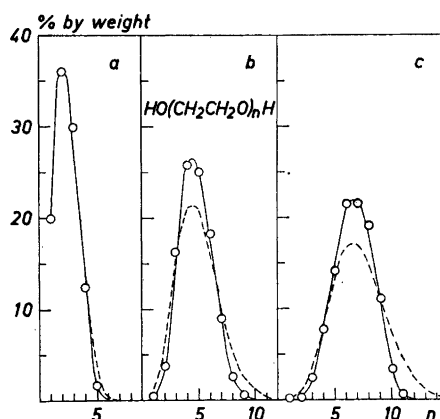


Fig. 2. Composition of polyethylene glycols derived from ethylene glycol. Average molecular weights: a) 109, b) 205, c) 297. (Expt. Nos. 4–6). Dashed curves represent theoretical compositions as calculated from the Poisson distribution.

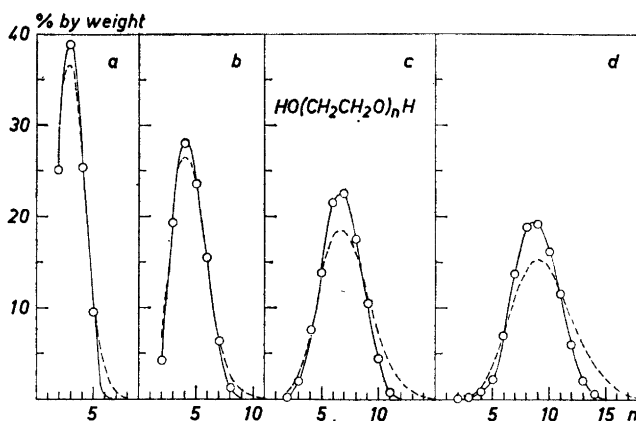


Fig. 3. Composition of polyethylene glycols derived from diethylene glycol. Average molecular weights: a) 151, b) 197, c) 304, d) 407. (Expt. Nos. 2, 9–11). Dashed curves represent theoretical compositions as calculated from the Poisson distribution.

ence in composition was found in the concentration range investigated (0–0.2 %). Thus, the amount of catalyst used in the oxyethylations does not seem to influence the molecular weight distribution.

Fig. 2 shows the composition of polyethylene glycols in the 100–300 molecular weight range, obtained by oxyethylation of ethylene glycol. Similar representation of the distribution of polyethylene glycols derived from diethylene glycol is given in Fig. 3. It is obvious from these figures that the composition agrees closely with the one calculated from the Poisson function only in the examples with a very low degree of polymerisation.

#### DISCUSSION

The gas chromatographic method presented is capable of giving quantitative information, with reasonable accuracy, on the composition of polyethylene glycols in the 100–400 molecular weight range. Therefore, the observed difference between the observed distribution of the components and the Flory theory is believed to be significant. A similar difference was in fact observed also by Almin when applying countercurrent distribution technique on polyethylene glycols in the 1500–6000 molecular weight range.<sup>8</sup>

The observed deviation from theory indicates that the reactivities of the various hydroxyl groups in the reaction mixture are slightly different. Thus, a narrower distribution than predicted from the Flory theory would be the result, if the hydroxyl groups in the longer polyether chains react more slowly than those in the shortest members. This possibly may be due to steric effects.

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